How to remove bias in genomic predictions ?

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Lactation stage dependent genome wide effects on breeding values in Holstein Friesians

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Phenotypic time dependency in milk production traits in dairy cattle has been known and analyzed over the last century. A genome wide study was conducted to investigate differences and changes in allele effects during the early lactation based on estimated breeding values (EBV). EBVs for milk yield, fat and protein yield, and fat and protein content of 2,408 German Holstein Friesian bulls were assessed in 10-day intervals for the first 60 lactation days (VIT Verden, Germany). EBVs were available for the first three lactations. The genotypic information was taken from the bovine 50k BeadChip (Illumina). 2,338 animals and 43,588 markers passed quality control (MAF <0.01, call rate <0.9, FDR <0.01, IBS<=0.95). The Bonferroni correction was applied to account for multiple testing and the λ inflation factor corrected for population stratification. Most markers were identified for fat content followed by fat yield and protein content. No significant markers were detected for protein yield. Almost all markers occurred on chromosome 14 around the DGAT1 gene. Additionally, single markers were found on chromosome 27 for fat content and chromosome 6 for protein content. Allele effects and P-values increased with later lactation days. One exception for the allele effects was fat yield where only minor differences but with a tendency to smaller effects were found for later lactation days. The most dramatic increase in allele effects and P-values was observed for protein content. Considering trend lines, a change in the slope of 10-18 units for effects on protein content was found, whereas effects on milk yield and fat content only changed for about 8-11 and 3-5 units, respectively. This study provided evidence that gene effects get more pronounced with progressing lactation, and loci with bigger effects at the beginning also tend to stronger affect the production in later lactation.
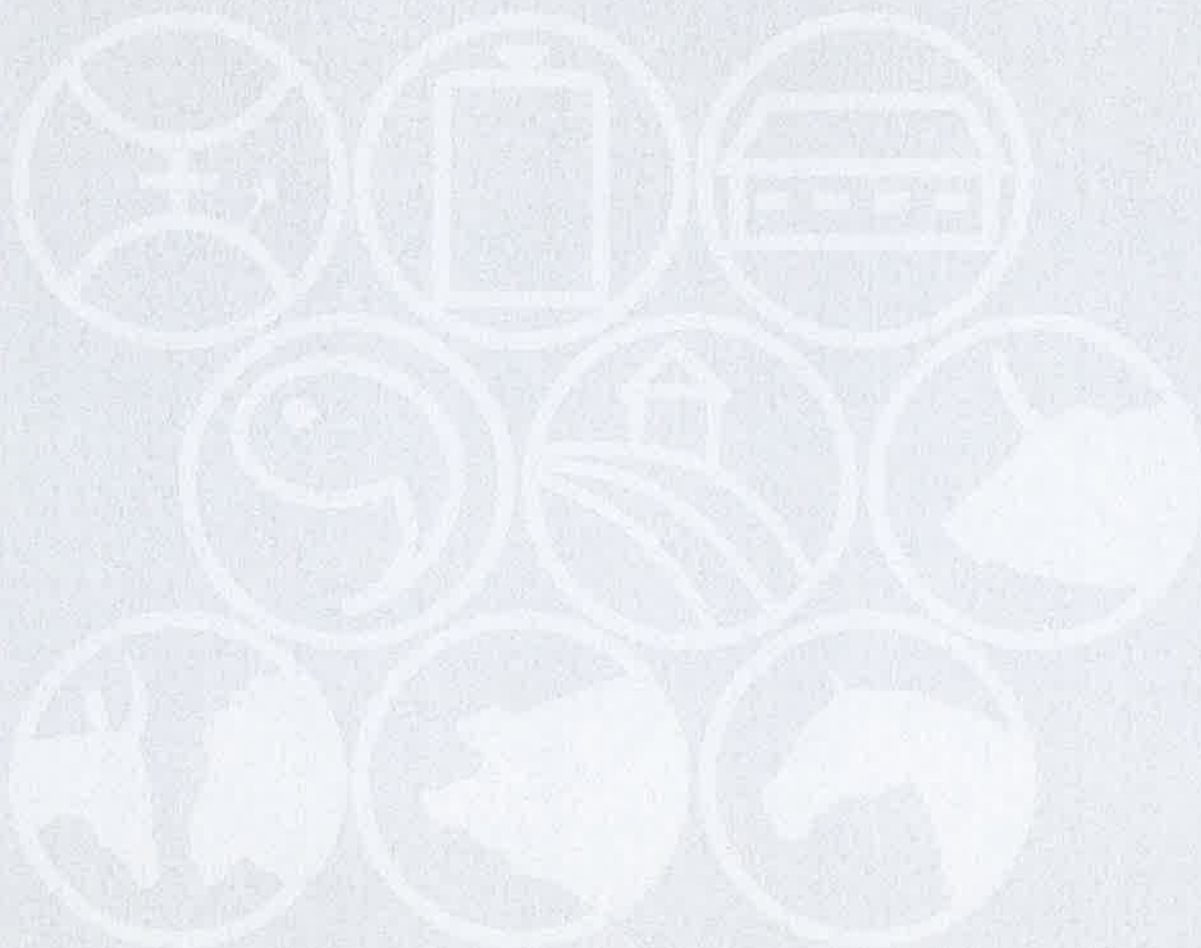

How to remove bias in genomic predictions?

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Unbiased predictions are of paramount importance in selection for accurate estimates of the genetic trend and also comparison of animals across generations. A single-step method, that combines all available data jointly (pedigree and genomic information), has been recently developed. This method is based on a pedigree relationship matrix augmented with genomic information. Since the model includes the data used for selection there are in principle no problems with biases from selection. However, bias was reported in genomic prediction and in genetic parameter estimates. If observed allelic frequencies are used, genotyped animals are considered the genetic base, but this does not correctly reflect the fact that genotyped animals are more related than expected in reference to the base population, especially if they are selected. For G to be correct, base allele frequencies would be required; this is unfeasible in practice. In this work we propose a method to remove bias of genomic prediction in the single-step procedure based on the correlation between the alleles within genotyped and nongenotyped individuals relative to the whole pedigree (Wright's F_{st}). We also evaluated the effect of the correction by simulation. The corrected G is an appropriate methodological solution that takes into account the effect of nonrandom genotyping and selection on prediction. The results clearly show that a corrected G within a single-step genomic prediction approach is able to include all data and remove bias due to selection.

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